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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,701	02/25/2000	JOHN P. LEONARD	GI5229FWC-DIV1	7087

25291 7590 01/30/2003

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/30/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/512,701	LEONARD ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication app ars on the cover sh t with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 5 sheets
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicants' Response filed October 16, 2002 is acknowledged and has been entered. Claims 16-31 are now pending in the present application. Applicants' references submitted on October 22, 2002 are acknowledged and have been added to Form PTO-892, so that they will become part of the official record of this application. All rejections have been withdrawn in view of Applicants' Response with the exception of those discussed.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 23, 24, 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using an IL-12 antibody, does not reasonably provide enablement for use of an antibody binds to a 40 kD or 35 kD subunit of IL-12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification has not taught such an antibody that only binds to the 40 kD or 35 kD subunit of the IL-12 and will still be able to treat rheumatoid arthritis in a human. Further, the specification is not enabled for the scope of claims 30 and 31, which are directed, methods of treating rheumatoid arthritis by administering IL-12 antagonists in combination with other therapies for autoimmune conditions; therapies comprise steroidal or other anti-inflammatory therapies.

The rejection is maintained for the reasons of record. Applicant's arguments filed October 16, 2002 have been fully considered but they are not persuasive. Applicants have asserted that the specification provides an example of how IL-12 antibody can be used to treat an animal model of MS showing that it does, in fact, decrease levels of IFN- production, and that one of skill in the art would be able to use this invention as disclosed and optimize it with undue experimentation, to treat RA, another condition that benefits in the reduction of IFN- levels. Although the specification does not specifically set forth IL-12 antibodies administered to a animal or human to treat RA, it would be reasonable to one skilled in the art that IL-12 antibody could be used to treat RA in a similar manner as IL-12 antibody is used to treat MS, for the reasons given by Applicants. It would appear that the anti-IL-12 antibodies would decrease the IFN- production and thus be able to treat RA, since Applicants and the prior art suggest that IFN- production promotes several autoimmune conditions including MS and RA. The prior art suggests that IL-12 expression is required for disease progression (CIA, collagen-induced arthritis, an animal model of RA) and inhibition of IL-12 with mAb prevents disease progression (Peeva et al, 2000).

However, the specification does not enable the claims set forth in this rejection. Claims 23 and 24 are directed to treatment of RA by administering an antibody that binds to a 40 kD or 35 kD subunit of IL-12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification has not taught such an antibody that only binds to the 40 kD or 35 kD subunit of the IL-12 and will still be able to treat rheumatoid

arthritis in a human or animal. Applicants have pointed to portions of the specification for support that appear to be a mere paper protocol for a method of treating RA that administers an antibody that binds to a 40 kD or 35 kD subunit of IL-12 (IL-12 subunit "may be used"; pp. 6-8). Kim et al (2000) teaches that IL-12 levels reflect RA disease activity and that IL-12 is involved in the production of proinflammatory cytokines. An IL-12 blockade (i.e. anti-IL-12 antibodies) could be useful for the treatment of RA. Kim et al also teaches that the IL-12 is composed of the p35 and p40 subunits, but that neither of these (p35 or p40) subunits has been found to display any significant biological function alone (p. 175).

Applicants have also asserted that the specification finds support for combination therapies using IL-12antogaonists in combination with other therapies for autoimmune conditions as set forth in claims 30 and 31. However, the specification is not enabled for the scope of claims 30 and 31, which are directed, methods of treating an autoimmune condition by administering IL-12 antagonists in combination with other therapies for autoimmune conditions; therapies comprise other anti-inflammatory therapies. The specification states that the IL-12 antagonist may be administered alone or combined with other therapies for autoimmune conditions such as steroidal or other anti-inflammatory therapies and administering other cytokines. The examples of the specification set forth IL-12 antagonist administration to mice for the treatment of MS (Example 1) and IDDM (Example 2). There are no examples or demonstrations of enablement of methods of treating any autoimmune condition be administering IL-12 antagonist in combination with other therapies for autoimmune conditions such as steroidal or other anti-inflammatory therapies and administering other cytokines. What are

the other anti-inflammatory therapies or steroids that will be used, what are the dosage regimes etc, for these therapies? Do any of these other therapies counteract the effects of the IL-12 antagonist? The two examples of the specification do not set forth IL-12 antagonist administration with any other therapy. There does not appear to be any evidence in the specification that would indicate that these claimed combinations (anti-IL-12 antibodies and other therapies, steroids for example, for autoimmune conditions) would be effective to treat RA.

Although the art appears to indicate that anti-IL-12 antibody treatment would be beneficial in the treatment of RA; the art is not clear with regard to combination therapies, which include anti-IL-12 antibodies for the treatment of RA. Jaffe discusses that some combination drug therapies have not been successful (p. 25). Borigini et al teach that several factors have retarded progress in the search for successful combinations of DMARDS (disease-modifying antirheumatic drugs) such as toxicity, the evaluation and approval process in establishing combinations of agents, as well as random drug combinations and doses (p. 692; table 1; see also Verhoeven et al 1996). It is not clear what methods or protocols will be used. Does Applicant intend to use combinations of drugs given in a single dose at the outset (day 1), sequential studies which seek to demonstrate an additive effect of two different therapies, or some other method? (See also different strategies set forth by Borigini et al, p. 691). In view of the above there would be undue experimentation for a skilled artisan to practice the claimed invention.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-20 of co-pending Application No. 09/512930. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications claim methods of administering to a subject a therapeutically effective amount of an IL-12 antagonist (i.e. antibody immunoreactive with IL-12 or antibody fragment immunoreactive with IL-12); the antagonist is being administered for the purpose of treating conditions promoted by an increase in

levels of interferon-gamma, which encompasses autoimmune diseases such as rheumatoid arthritis or multiple sclerosis.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. No claims are allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nita M. Minnifield whose telephone number is 703-305-3394. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Nita M. Minnifield
Primary Examiner
Art Unit 1645

January 6, 2003